Resources for Latent TB Treatment

Testing Pearls

- The interferon gamma release assays (IGRAs, QuantiFERON Plus or T-SPOT.TB) are the preferred tests for most patients.
- Despite high specificity, when testing low-prevalence populations (most US-born people, for example), most positive tests will be false-positive. CDC guidelines therefore recommend repeating the test for low-risk people, and not offering latent TB treatment for people whose second test is negative.
- Screening prior to latent TB treatment should consist of a symptom screen, a chest radiograph, and a focused physical exam.
    - The most common site of active TB outside the lungs is the lymph nodes of the neck, so screening for cervical lymphadenopathy should be a routine part of the exam

Treatment of latent tuberculosis

- Short-course regimens are preferred for most patients
- The two commonly used short-course regimens are as follows:
    - Rifampin daily for 4 months
    - Isoniazid/rifapentine once-weekly for 12 weeks
- Both regimens can be given self-administered
- For patients with unacceptable drug interactions or intolerance of rifampin/rifapentine, isoniazid for 6-9 months is used (6 months is preferred in current guidelines, 9 months may be preferable for immunocompromised patients)
- Dosing for adults and children is in the table below

Drug Dosages for Treating LTBI		
Regimen	Dosage (maximum dose is listed in parenthesis)	
	Adults (age >12)	Children (age 12 and under) *
Rifampin 4 months daily	10 mg/kg (600 mg)	15-20 mg/kg (600 mg)
Isoniazid/rifapentine 12 weeks once-weekly* Isoniazid Rifapentine	15 mg/kg (900 mg) Weight — Dose 10.0-14 kg — 300 mg 14.1-25.0 kg — 450 mg 25.1-32.0 kg — 600 mg 32.1-49.9 kg — 750 mg ≥50 kg — 900 mg	25 mg/kg (900 mg) Child weight — Dose 10.0-14 kg — 300 mg 14.1-25.0 kg — 450 mg 25.1-32.0 kg — 600 mg 32.1-49.9 kg — 750 mg ≥50 kg — 900 mg
Isoniazid 6-9 months daily**	5 mg/kg (300 mg)	10-20 mg/kg (300 mg)

- The 4-month course of rifampin should be completed within 6 months
- At least 11 doses of once-weekly isoniazid/rifapentine should be completed within 16 weeks

- At least 6 months of isoniazid should be completed within 9 months (or 9 months within 12 months)

Best practices for safe prescribing:

- Rifampin and rifapentine have many drug interactions, generally mediated by induction of P450 enzymes with reduced efficacy of other medications
- Medications commonly affected by rifampin include oral contraceptives, antiretrovirals, warfarin, directly acting anticoagulants, and many antihypertensives
- Check interactions prior to prescribing—********reference.medscape.com/drug-interactionchecker is a useful reference
- Prior to initiating rifampin or isoniazid/rifapentine, obtain a baseline CBC with platelets, and hepatic function panel[1] on the following individuals:
    - average alcohol use of ≥ three drinks per day or binge drinking (≥ five drinks in one day, intermittently) (one drink is defined as one 12 oz beer, 4 oz of wine or 1 oz of liquor).
    - HIV positive.
    - Underlying liver disease.
    - Pregnant women.
    - Those currently taking other potentially hepatotoxic drugs such as:[1]
        - "statin" drugs;
            - atorvastatin (Lipitor)
            - cerivastatin (Baycol)
            - lovastatin (Mevacor)
            - pravastatin (Pravachol)
            - rosuvastatin (Crestor)
            - simvastatin (Zocor)
        - anticonvulsant drugs;
            - carbamazepine (Tegretol)
            - phenytoin (Dilantin)
            - valproic acid (Depakote)
        - methotrexate; and
        - miscellaneous antidiabetic agents for Type 2 diabetes.
            - pioglitazone (Actos)
            - rosiglitazone (Avandia)

b. If baseline CBC with platelets and liver function panel are outside normal limits, consult physician before initiating treatment for LTBI.

c. Obtain hepatic function panel monthly on the following individuals who are taking rifampin:

- Baseline hepatic function panel results are abnormal;
- Pregnant women;

[1] Note that this is an incomplete list of medications with potential for hepatotoxicity

- Women up to three months postpartum the immediate postpartum period (i.e., within three months of delivery);
- Persons with symptoms of adverse reactions;
- Persons taking potentially hepatotoxic drugs (above list);
- Persons with chronic active hepatitis B or those with hepatitis C;
- Chronic or binge use of alcohol; and
- Persons living with HIV infection.

- Prescribe only one month at a time of medication. The patient should call the office a few days before the end of the month to verify that they are taking the medicine, not having side effects, and are willing to continue. If monthly laboratory monitoring is indicated, a lab visit can be set up when the patient calls.
- It is common practice to give 1 month of latent TB treatment prior to starting biologics, mostly to assess tolerability of the latent TB therapy
- Common side effects of latent TB treatments:
    - Hepatotoxicity (all regimens).
        - ♣ Mild transaminase elevation is common but often resolves spontaneously. Therapy should be stopped if the ALT is >3x the lab upper limit of normal if the patient is symptomatic (e.g. nausea, vomiting, dark urine, abdominal pain) or if the ALT is >5x the upper limit of normal without symptoms
    - Flu-like syndrome (rifampin, isoniazid-rifapentine)
        - ♣ Fever and myalgias sometimes accompanied by thrombocytopenia, typically happens a few hours after the medication is taken
        - ♣ Usually discontinuation of the latent TB regimen is necessary
    - Cholestasis (rifampin, isoniazid/rifapentine)
        - ♣ Elevated bilirubin/alk phos with normal transaminases and no other etiology
        - ♣ Resolves after medication is discontinued
        - ♣ Often recurs with rechallenge
    - Hypotension (isoniazid/rifapentine)
        - ♣ Can present with syncope, usually soon after taking dose
        - ♣ Discontinuation of the regimen is recommended

A couple of EPIC-style dot phrases are included on the following pages and can be pasted into patient education materials.

Feel free to reach out with any questions—email is best, Jason.stout@dm.duke.edu.

.latenttb

You have been diagnosed with latent tuberculosis infection ("latent TB"). Latent TB is a condition in which you were previously exposed to the germ that causes tuberculosis but are not sick. Exposure typically occurs when a person breathes the same air as a person who is sick with tuberculosis.

People with latent TB are well and are not contagious. However, the TB germ often is lying dormant in people with latent TB. The germ can wake up and make people sick many years after infection. While the germ can wake up and make a healthy person sick, people with conditions that suppress the immune system are more likely to have the germ wake up and make them sick.

There are medicines available to treat latent TB. Treating latent TB reduces the risk of getting sick in the future by 80-90%. Taking the medicines will not make the skin test or blood test used to diagnose latent TB negative, so getting another test after treatment is not useful.

.rifampin

You have been prescribed a medication called rifampin to treat your latent tuberculosis. Rifampin is an antibiotic that kills the germ that causes tuberculosis. Taking this medication as prescribed can reduce the risk of getting sick in the future. You will need to take the medicine every day for about four months. If you miss a day, just take the medicine as usual the next day.

Like any medication, rifampin can have side effects. Common side effects may include the following:

- Nausea
- Vomiting
- Diarrhea
- Red- or orange-colored urine (this is normal, it is just the color of the medication)
- Skin rash
- Fevers
- Body aches

Let your provider know right away if you have any of these side effects, as they may sometimes indicate a more serious problem related to the medicine. Rifampin can also interact with many other medicines, so let your provider know if you start any new medicines, even over-the-counter.

Rifampin is often better tolerated when taken with food.

.inhrifapentine

You have been prescribed two medicines called isoniazid and rifapentine to treat your latent tuberculosis. These are two antibiotics that kill the germ that causes tuberculosis. Taking this medication as prescribed can reduce the risk of getting sick in the future. You will need to take

the medicines all together at the same time once a week for twelve weeks. If you forget to take the medicine on the usual day, it is fine to take it on the next day.

Like any medications, isoniazid and rifapentine can have side effects. Common side effects may include the following:

- Nausea
- Vomiting
- Diarrhea
- Red- or orange-colored urine (this is normal, it is just the color of the medication)
- Skin rash
- Fevers
- Body aches
- Dizziness or fainting

Let your provider know right away if you have any of these side effects, as they may sometimes indicate a more serious problem related to the medicine. These medications can also interact with many other medicines, so let your provider know if you start any new medicines, even over-the-counter.